SUMMARY OF INTERVIEW

Applicants wish to thank Examiner Prats for the personal interview conducted on August 4, 2005 with Julian Reid and Andrew Merickel. Distinctions between the presently claimed invention and the processes disclosed in the Ju and Davis references were discussed, along with the distinction between whey protein concentrate (WPC) and whey protein isolate (WPI). The amendments and comments herein are consistent with that discussion.

REMARKS

Claims 1-19, 22-30 and 32-36 are pending in the application. Claim 2 is canceled herein. In addition, Claim 1 has been amended to indicate that the whey protein isolate is hydrolyzed with Neutrase. Support for this amendment can be found, for example, in Example 1 of the Specification and in original Claim 2. Claim 7 has been amended to be consistent with Claim 1. In addition, Claim 1 has been amended to recite an enzyme to substrate ratio between about 0.01% and about 3% w/w total solids. Support for this amendment can be found, for example, at page 5, lines 1-5 of the specification. These amendments do not add new matter.

Claim Rejections Under 35 U.S.C. § 102

Claims 1, 2, 7, 13-18, 22-23, 27-29 and 32-34 were rejected under 35 U.S.C. § 102(b) as being anticipated by Ju et al. (J. Dairy Sci. 78:2119-2128 (1995)). The Examiner found that Ju discloses the hydrolysis of WPI with three different neutral proteases at pH 7 and 40°C, with the reaction being stopped by dilution and pH change to 2.5. The Examiner concluded that because Ju contacts the same substrate with the same enzyme under the same conditions, a holding of anticipation of the claims is required.

Claim 1 has been amended to indicate that the enzyme to substrate ratio in the claimed process is from about 0.01% to about 3% w/w total solids. In contrast, the process disclosed in Ju uses an enzyme to substrate ratio of 10% w/w for Neutrase (page 2120 second column). There is no teaching or suggestion in Ju of using an enzyme to substrate ratio between 0.01% and about 3% w/w total solids when using Neutrase. Thus, Ju can not anticipate the present claims.

The Examiner noted that Ju was considered to anticipate those claims reciting specific peptides, and presumably the product by process claims, because the same starting material was combined with the same enzyme and subjected to the same hydrolytic conditions. The Examiner concluded that the same result must inherently have occurred and that the hydrolysate produced by Ju must inherently have the same composition, including the specific peptides recited in the claims.

As discussed above, Claim 1 has been amended to indicate that the enzyme to substrate ratio is between about 0.01% and about 3% w/w total solids. As this feature is not taught by Ju,

the hydrolysate produced by Ju would not inherently be the same and would not inherently produce the same hydrolysate or contain the recited peptides.

In addition, there are a number of other differences between the method disclosed in Ju and the process disclosed in the present application that produced the recited peptides. These differences provide further indication that the Ju process would not inherently produce the recited peptides.

First, Ju uses 10% Neutrase while the process disclosed in the present application used 0.9% Neutrase (see Examples 1 and 6). This is a greater than 10-fold increase in the amount of enzyme used in Ju compared to the disclosed process, a significant difference that will inevitably lead to a difference in the peptide profile of the resulting hydrolysate. This is because during any hydrolysis reaction, the most accessible cleavage sites on the proteins are on the outside of the protein molecules and are cleaved first to produce primary peptides. The primary peptides are then cleaved to form secondary peptides. The rate of conversion of primary peptides to secondary peptides is proportional to the enzyme concentration and will thus occur at a higher rate in the Ju process than in the process disclosed in the present application. At pages 2122-2123, Ju observes that Neutrase causes the highest degree of hydrolysis, yet left more intact protein (β-lactoglobulin and α-lactalbumin) than the hydrolysates prepared using other enzymes. Ju explained this observation by the ability of Neutrase to liberate high numbers of small peptides and amino acids. This is consistent with the conversion of primary peptides to secondary peptides. In contrast, in the process disclosed in the present application, there will be a predominance of primary peptides.

In addition, Ju uses a reaction temperature of 40°C while the reaction temperature used in the process in Example 1 is 50°C. The difference of 10°C is significant in reaction terms as the temperature has a significant effect on the makeup of the resulting hydrolysate. In particular, temperature is important in terms of the amount of unfolding of the proteins in the reaction mixture. The higher the temperature, the higher the degree of protein unfolding that will occur. Thus, at the higher temperature, there will be more unfolding of proteins, which causes a shift in protein conformation and the exposure of additional protein cleavage sites that would not be exposed in the more folded proteins in the Ju reaction mixture. This results in the generation of peptides in the disclosed process that would not be present in the Ju hydrolysate.

Further, the process of Ju uses a 12% substrate concentration during hydrolysis while the process disclosed in Example 1 of the present application used a 4% substrate concentration. Ju apparently used such a high concentration because they were concerned with the gelling properties of hydrolyzed WPI. Ju provides evidence that gel formation is the result of protein/protein interactions. Weak gel formation begins to occur at around 9% substrate concentration and by 12% there are significant levels of protein/protein interactions. The high substrate concentration will impact the final peptide profile of the hydrolysate. In particular, the greater the amount of protein/protein interaction, the more protein cleavage sites will be masked and unavailable to the enzyme, even when the enzyme concentration is very high. Protein/protein interactions are also known to cause conformational changes. Thus, the process of Ju will inevitably result in a different peptide profile in the final hydrolysate from the process disclosed in the present application.

As a result of the differences in the reaction conditions disclosed in the process of Ju and in the process disclosed in the present application, Ju does not inherently produce the claimed hydrolysate, or the bioactive peptides that are presently recited in the claims. Each of the four differences in the reaction conditions of Ju on its own presents a major factor that will alter the peptide content of the hydrolysate. Taken together, it cannot be predicted, with any certainty, that the peptide hydrolysate produced by Ju will be the same as that produced by the claimed process. Thus, Ju cannot inherently anticipate the claims and Applicants request withdrawal of the rejection.

For the reasons present above, Applicants submit that Ju et al. does not anticipate the present claims and request withdrawal of the rejection.

Claims 1, 3, 5, 6, 13-19, 22, 23, 27-30 and 32-36 were rejected under 35 U.S.C. § 102(e) as being anticipated by Davis (U.S. Patent No. 6,630,320). The Examiner found that Davis discloses the hydrolysis of whey protein isolate with the neutral protease porcine trypsin and concludes that because Davis contacts the claimed substrate with the claimed enzyme under the claimed conditions and uses the product to treat hypertension, a holding of anticipation is required.

Applicants have amended Claim 1 to indicate that the WPI is hydrolyzed with the enzyme Neutrase. Davis has no teaching or suggestion to use the enzyme Neutrase. In this regard,

Applicants note that the claims of the Davis patent are directed to the treatment of hypertension by administering a WPI hydrolysate that has been prepared using trypsin. In the examples in Davis, a trypsin hydrolysate (601K) was effective at reducing arterial blood pressure while hydrolysates produced using other proteases were not effective and did not change arterial blood pressure. Thus, according to Davis the desired bioactivity is only obtained from a trypsin WPI hydrolysate. As a result, Davis teaches away from the presently claimed invention because a skilled worker would not be motivated to use other proteases, such as Neutrase to produce a hydrolysate comprising bioactive peptides in view of Davis.

In view of the lack of teaching or suggestion in Davis of a hydrolysate prepared using Neutrase, Applicants submit that the claim rejections should be withdrawn.

Claim Rejections Under 35 U.S.C. § 103

Claims 1-19, 22-30 and 32-36 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Schlothauer (WO 99/65326) in view of Ju. In making the rejection, the Examiner notes that Schlothauer is different from the present invention as it is directed to the hydrolysis of WPC rather than WPI. This is a crucial difference and there is no teaching or suggestion in Schlothauer or Ju that would suggest replacing the WPC in the Schlothauer process with WPI. The WPI hydrolysate of the present invention was superior over the WPC hydrolysate of Schlothauer in terms of its bioactivity, flavour and functionality. This was a totally unexpected result.

A WPC is produced from whey, which is a by-product produced in cheese manufacturing plants. The whey by-product comprises a solution of fat, all of the milk GMP, all of the milk whey proteins, lactose, some casein fragments, minerals etc. To make a WPC, the whey by-product is first ultrafiltered to concentrate the solids. Some of the fat and mineral components and some casein fragments may also be filtered out, but overall the solids composition of the ultrafiltrate and the whey starting material are similar. The ultrafiltrate is then dried to form a WPC. The WPC comprises approximately 60% whey proteins.

To make a WPI, a WPC is used as the starting material and is subjected to ion exchange chromatography. This purification step removes everything except the whey proteins α-lactalbumin and β-lactoglobulin. The final WPI product comprises purified (90%) α-

lactoglobulin and β-lactalbumin with no other impurities (such as minerals, fat, casein fragments, other whey proteins, GMP etc which are present in significant amounts in WPC).

The superior results achieved in the presently claimed invention using WPI were unexpected because it is known that casein peptides are biologically active. Thus, it would have been expected that a WPC hydrolysate (which contained casein fragments) would produce bioactive peptides. On the other hand, a WPI, which does not contain casein fragments, would not be expected to produce a hydrolysate that would have the same or better biological activity. That is, the knowledge of the skilled artisan would teach away from the present invention as WPI does not contain any casein.

Consistent with this understanding of the differences between WPC and WPI, there is no teaching or suggestion in Schlothauer to substitute WPI for WPC. Ju is directed to the gelling properties of WPI hydrolysates and has no teaching or suggestion of creating hydrolysates with bioactivity. Thus, Ju also fails to provide any motivation for the combination cited by the Examiner. In view of the lack of motivation to replace WPC with WPI in the process of Schlothauer, and the unexpected results obtained by the claimed invention, Applicants submit that the present rejection should be withdrawn.

The Examiner also rejected claims 1-19, 22-30 and 32-36 as obvious over the combination of Schlothauer and Davis. Again, Applicants respectfully disagree.

The claimed process is directed to the use of Neutrase to produce a WPI hydrolysate having bioactivity. Davis teaches a skilled worker that neutral proteases other than trypsin do not produce bioactive hydrolysates from a WPI starting material. Thus, Davis teaches away from the present invention and does not provide any teaching or suggestion for substituting WPI for the WPC used in Schlothauer. In view of the lack of motivation for the combination of Schlothauer and Davis, Applicants request withdrawal of this rejection as well.

Conclusion

In view of the amendments and arguments presented above, Applicants submit that the present Application is in condition for allowance and respectfully request the same. If any issues remain, the Examiner is invited to contact Applicants' representative at the number provided below in order to resolve such issues promptly.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

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By: _____

Andrew N. Merickel
Registration No. 53,317
Attorney of Record
Customer No. 20,995
(415) 954-4114

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